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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/322,732	05/28/1999	KEITH R. MAROTTI	PUJ-0041	8413

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/322,732	MAROTTI ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,143-146 and 151-163* is/are pending in the application.

4a) Of the above claim(s) *151-153 and 155-163* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *7,8,143-146 and 154* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to the Office Action mailed November 26, 2003 on March 26, 2004 is acknowledged.

Claim Disposition

2. Claims 1-6, 9-142 and 147-150 have been canceled. Claims 151-163 have been added. Claims 7-8 and 143-146 have been amended. Claims 7-8, 143-146, and 151-163 are pending. Claims 7-8, 143-146, and 154 are under examination. Claims 151-153 and 155-163 are withdrawn from consideration as directed to a non-elected invention.

3. Newly submitted claims 151-153 and 155-160 are directed to "a method for identifying a compound that binds to efp and a method for detecting binding of a putative efp-binding compound" which are separate from the method examined which is "a method for identifying a compound that increases an activity of efp". The newly submitted methods have different objectives and method steps. Note that the elected invention which was not traversed, and is directed to a method of identifying a compound that alters efp binding activity such that an increase results and increases an activity of L16, not to a method to identify a compound that binds efp or detect binding of a putative efp-binding compound". Regarding claims 161-163 the method is to

identify a compound that modulates the binding of efp, however, the method includes a step that involves "determining whether the compound modulates the binding of said bound compound, thus this method involves a different step than the one examined which involved determining if the compound modulates/alters/increases the binding activity of efp, not identifying a compound and determining if said compound modulates the binding of said compound. Since the method claims as submitted are directed to an invention that is independent or distinct from the invention originally claimed for the reasons indicated above and since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. The newly submitted claims would have been subjected to a Restriction Requirement had they been presented at the time of filing.

Specification

4. The disclosure is objected to because of the following informalities:

The specification is objected to because trademarks are disclosed and they are not capitalized. The use of the trademark such as Tween-20, Tris-HCL etc., has been noted in this application (see page 25). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be

respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 7-8, 143-146 and 154 are rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabled for the full scope of the claims, for example a method for identifying a compound (unlimited) that increases the binding activity of efp by contacting efp with a compound (unlimited). The specification is enabled for a binding assay using radiolabeled oxazolidinone bound to efp (such as linezolid or eperezolid) see pages 15+ of the specification. The claimed invention is also enabled for the prior art teachings of compounds (antibiotics such as chloramphenicol, lincomycin, etc.) that inhibit binding to the 50S ribosomal subunit. However, the specification is not enabled for a method with an unspecified amount of compounds that are expected to not only bind efp, but alter efp to produce increase binding activity and

alter the L16 protein to increase an activity (unspecified) in the L16 protein, as the specification does not exemplify such a method. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in the art, predictability or unpredictability of the art and breadth of the claims, these factors are addressed below.

The claimed invention is directed to a method which encompasses any and all possible compounds and a method step that utilizes the unidentified compound in the process and a method that does not identify the specific L16 activity or the nexus between an increase in binding of efp and an increase in L16 activity. The claimed method does not provide steps to address compounds that may bind efp and have no effect on the L16 protein or *vise versa*. Moreover, the claimed method of identifying a compound that increases binding in efp has an end result to determine whether a compound increases activity of efp and a L16 protein. The method recited in the claims provides no indicia how you can go from a preamble of identifying a compound that increase efp binding activity and result in an increase in L16 protein activity, said activity is not recited in the claim. One of skill in the art would have to engage in undue experimentation to determine if compounds for example, those found in a Merck catalog will bind efp and if said compounds will alter efp such that an increase in binding results.

Then further investigate to determine if the same compounds have an effect on a L16 protein such that there is an increase in an activity and determine what that activity is, absent guidance/direction in the instant specification. The claimed method is also unpredictable as non-specific binding could occur, binding may not occur directly and although binding occurs the compound may not alter an activity for efp or the L16 protein.

The nature of the claimed invention is a method which includes steps to contact an unknown compound with efp, then determining if said compound increases activity of efp which implies that all the possible compounds encompassed in the claimed invention will directly bind to efp during contact and once bound will increase efp activity and an activity of a L16 protein. There is no method step to describe how to get a compound to bind to efp indirectly and no discussion of compounds that may bind efp but may not increase efp binding activity. The specification describes the claimed invention as a binding assay, however, the specification provides only examples and no specific assays to accompany the claimed method. Additionally, the specification asserts that the claimed method will identify a compound that modulates the activity of prokaryotic efp, determine whether the compound modifies activity of efp, for example determining if the compound binds to efp by a number of art-recognized procedures (i.e., binding assays such as gel-shift mobility electrophoresis, Western blot, filter binding and scintillation proximity assay). Note that the claimed method is relying on art-recognized procedures, yet the specification asserts that this is a new method/procedure. Moreover, claim 154 recite a method wherein a compound

modulates efp binding activity and it is unclear if the binding activity of efp will increase or decrease, what conditions will be suitable for efp to bind to the unknown compound and how to detect modulation of binding activity by an unspecified amount of compounds. Furthermore, the information provided in the specification is exemplary and not limiting, therefore, does not breathe life into the claims. In view of the foregoing, one of skill in the art would have to engage in undue experimentation to be able to practice the full scope of the claims since the specification does not provide sufficient detail.

In the absence of sufficient guidance/direction regarding the steps to determine whether the test compound modulates the activity of efp one skilled in the art would not be able to practice the claimed invention commensurate in scope with the claims. Further, the claimed methods do not have endpoints/results that correspond to the preamble of the claims, thus, it doesn't appear that the objective of the method is obtained. In fact the claims read on a binding assay rather than a method to identify a compound that has the desired effect on efp or the L16 protein. In addition, the claims broadly recite a method of identifying a compound that modulates efp binding activity, however, there is no specific assay and measurements to obtain this information nor information as to whether modulation is up or down (see claim 154 for example). Note for example that the prior art teaches that genes encoding certain ribosomal proteins can be deleted from the chromosome without an apparent effect on cell viability. It is also stated that most initiation, elongation and termination factors are required for cellular growth, however, some of these proteins may be dispensable under certain

growth conditions (Aoki et al., The Journal of Biological Chemistry, vol. 272, no. 51, 1997). Further, in a binding study performed by Lin et al., (Antimicrobial agents and Chemotherapy, vol. 41, no. 10, pages 2127-2131, October 1997) it was found that Oxazolidinone eperezolid binds to the 50S ribosomal subunit and competes with binding of chloramphenicol and lincomycin. The study demonstrates that these compounds inhibit binding to the 50S (also known as L16) subunit as the compounds block the initiation, elongation or termination phase of prokaryotic translation, the prior art does not support an increase in binding activity. Note that the instant specification on page 3 list several antibiotics known to inhibit translocation and occupation of a specific site on the ribosomes, however, has no effect on efp reaction. As there is no analogous art, the instant specification should provide adequate direction/guidance to practice the claimed invention to enable a skilled artisan to perform the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 7 and 144 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite because the claim is missing a transitional phrase where the claim recites "...increases binding activity of prokaryotic elongation factor p" The claim

should be amended to recite "...increases the or a binding activity of prokaryotic elongation factor p" (see also claim 144). The claim is also indefinite because step (c) is determining whether said compound that increases the activity of efp increase an activity of a L16 protein" yet the preamble of the claim is to identify a compound increasing efp binding activity. The claim should be amended to include the L16 protein in the preamble. The claim also lacks antecedent basis as the preamble is directed to "increases binding activity of efp" and items (b) and (c) recite "increases activity of efp".

7. Applicant's arguments filed on March 26, 2004 have been fully considered however, the rejections under 35 U.S.C. 112, first and second paragraph remains. Regarding the rejection under 35 U.S.C. 112, second paragraph the response on page 9 states that the claims have been amended to recite "binding activity" said amendment does not address the missing transitional phrase or the lack of correlation between the preamble and the end result of the method. With regard to the rejection under 35 U.S.C. 112, first paragraph applicant states that the claims have been amended to advance prosecution to recite "binding activity" (see page 8 of the response). However, the rejection remains because the amendment to the claims only addresses one issue raised previously (what activity of efp is being increased?), however it does not address what activity of the L16 protein is being increased, the lack of correlation between the preamble and the end result and the issue of will all possible compounds bind efp and alter efp, to name a few. Since activity refers to a variety of measurable indicia how does one skilled in the art determine what activity will be affected by the method with

regard to the L16 protein. In addition, the specific compound (oxazolidinone-eperezolid) disclosed in the instant specification to effect the claimed increase in efp binding activity and the L16 protein activity is known in the art to inhibit protein synthesis by inhibiting initiation phase of translation and is disclosed as having a dose dependent specific binding action wherein the dose of the compound is proportional to the ribosome concentrations (see Lin et al., 1997), therefore, it appears that binding may not occur or be direct, thus an increase in binding activity would not result. Therefore, for these and all other reasons stated above, the claimed invention is not enabled for the full scope of the claims. Thus, the rejection remains. Note that the rejection under 35 U.S.C. 112, first paragraph has been modified to incorporate newly submitted claim 154 and the 112, second paragraph rejection has been instituted based on amendments made and issues that remain.

Conclusion

8. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope A. Robinson, MS

Patent Examiner

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